UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

JAZZ PHARMACEUTICALS IRELAND LIMITED, Plaintiff, v. LUPIN INC., LUPIN PHARMACEUTICALS, INC., and TEVA PHARMACEUTICALS, INC., Defendants.	**Civil Action No. 21-14271 (SRC)** **OPINION & ORDER**

CHESLER, District Judge

This matter comes before the Court on the motion to amend the Answer by Defendants Lupin Inc., Lupin Pharmaceuticals, Inc., and Teva Pharmaceuticals, Inc. (collectively, "Defendants"). Plaintiff Jazz Pharmaceuticals Ireland Limited ("Plaintiff") has opposed the motion. For the reasons that follow, the motion will be denied.

Defendants have moved to amend the Answer to include a counterclaim for unenforceability of U.S. Patent No. 11,426,373 (the "'373 patent") due to inequitable conduct during prosecution. Claim 1 of the '373 patent is the sole independent claim:

> 1. A method of reducing food effect due to administration of gamma-hydroxybutyrate (GHB) in a patient having cataplexy in narcolepsy or excessive daytime sleepiness in narcolepsy, comprising:
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> orally administering to a patient in need thereof a pharmaceutically effective amount of a pharmaceutical composition of GHB in a unit dosage comprising at least one salt of GHB and a pharmaceutically acceptable carrier within four hours after eating;
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> wherein the pharmaceutical composition of GHB has reduced food effect as measured by C_{max} compared to an equal dose of immediate release liquid solution of Na.GHB, wherein the pharmaceutical composition

> comprises: about 5% to about 10% of Na.GHB; about 20% to about 25% of K.GHB; about 45% to about 50% of Ca.$(GHB)_2$; and about 20% to about 25% of Mg.$(GHB)_2$.

In opposition, Plaintiff argues that the motion should be denied because the amendment is futile and would not survive a motion to dismiss under Rule 12(b)(6). The Third Circuit has held:

> Leave to amend is properly denied if amendment would be futile, i.e., if the proposed complaint could not withstand a renewed motion to dismiss. In assessing 'futility,' the district court applies the same standard of legal sufficiency as applies under Rule 12(b)(6).

City of Cambridge Ret. Sys. v. Altisource Asset Mgmt. Corp., 908 F.3d 872, 878 (3d Cir. 2018) (citations omitted). Plaintiff aptly quotes the Third Circuit's decision in Sweda:

> We now turn to the task of evaluating [Plaintiffs'] complaint. We progress in three steps: First, we will note the elements of a claim; second, we will identify allegations that are conclusory and therefore not assumed to be true, and; third, accepting the factual allegations as true, we will view them and reasonable inferences drawn from them in the light most favorable to [Plaintiffs] to decide whether "they plausibly give rise to an entitlement to relief." Pleadings that establish only a mere possibility of misconduct do not show entitlement to relief.

Sweda v. Univ. of Pa., 923 F.3d 320, 326 (3d Cir. 2019) (citations omitted.) "A claim has facial plausibility when the plaintiff pleads factual content that allows the court to draw the reasonable inference that the defendant is liable for the misconduct alleged." Ashcroft v. Iqbal, 556 U.S. 662, 678 (2009).

Following the Third Circuit's guidance in Sweda, the Court begins the analysis by noting the elements of a claim for unenforceability of a patent due to inequitable conduct. The Federal Circuit has summarized the fundamental principles of such a claim as follows:

> To prove inequitable conduct, the challenger must show by clear and convincing evidence that the patent applicant (1) misrepresented or omitted information material to patentability, and (2) did so with specific intent to mislead or deceive

> the PTO. *Therasense, Inc. v. Becton, Dickinson and Co.*, 649 F.3d 1276, 1287 (Fed. Cir. 2011) (en banc). Materiality and intent must be separately established. *Id.* at 1290. To establish materiality, it must be shown that the PTO would not have allowed the claim but for the nondisclosure or misrepresentation. *Id.* at 1291. To establish intent, intent to deceive the PTO must be "the single most reasonable inference able to be drawn from the evidence." *Id.* at 1290.

In re Rosuvastatin Calcium Patent Litig. v. Aurobindo Pharma Ltd., 703 F.3d 511, 519 (Fed. Cir. 2012). As to the materiality requirement, the Federal Circuit has held:

> [A]s a general matter, the materiality required to establish inequitable conduct is but-for materiality. When an applicant fails to disclose prior art to the PTO, that prior art is but-for material if the PTO would not have allowed a claim had it been aware of the undisclosed prior art.

Therasense, Inc. v. Becton, Dickinson & Co., 649 F.3d 1276, 1291 (Fed. Cir. 2011).

In considering the issue of whether the proposed Counterclaim would survive a Rule 12(b)(6) motion, a key question is whether the Counterclaim plaintiff has pled sufficient facts to allow this Court to infer that it is plausible that the requirements for materiality may be satisfied. Pursuant to Therasense, the facts must make plausible the inference that, but for the omitted information, the PTO would not have allowed the claims of the '373 patent.

Defendants' proposed Counterclaim pleads facts to support, broadly, two theories of inequitable conduct during prosecution of the '373 patent: 1) the applicants withheld from the PTO particular material information that had been submitted to the FDA as part of the related new drug application, especially variability data (the "error bars") for Figure 1; and 2) the applicants withheld particular material prior art references contained in the Wilding email.

I. The theory of inequitable conduct based on differences between FDA and PTO submissions

What follows is a selection of the key allegations in the proposed inequitable conduct Counterclaim that underpin Defendants' first theory of inequitable conduct, predicated on withholding material information that had been submitted to the FDA:

> 227. At the Examiner Interview, Mr. Allphin argued that the claimed invention using a mixture of salts "obtains a surprising effect compared to XYREM (Na-GHB)" and had less of a food effect. *Id.* Mr. Allphin was the only inventor listed on the '373 patent who participated in that (or any) interview. *Id.* A notice of allowance issued two months later citing the information provided by Mr. Allphin as one of the reasons for allowance. *See* JPIL0179414-417 ('373 patent FH, May 9, 2022 Notice of Allowance).
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> 229. At his deposition, Mr. Allphin testified that "in order to know how reliable data are, you'd have to know two things; the error bars, the variance, as well as the sample size. It's a statistical evaluation. For a layperson, an error bar gives you a rough idea of how much variation there was in the results that you got." Allphin Dep. at 217:25-218:18. Yet when he prepared the data figures for the USPTO from Jazz's dataset which contained error bars and was, with error bars submitted to the FDA, he omitted the error bars showing broad statistical deviations that had been presented to FDA . . .
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> 230. Instead, Mr. Allphin prepared Figures with no error bars or any other indicia of standard deviation, standard error, range or confidence interval for the '373 patent. . .
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> 231. Omitting those error bars along with any other indicia of the broad deviation in the data, Mr. Allphin misleadingly presented the data to the Patent Office. These withheld statistical data are material because the Patent Office would not have allowed the claims of the '373 patent had it been aware of those data. This is confirmed by at least Mr. Allphin's own testimony, admitting that "in order to know how reliable data are, *you'd have to know two things*; the error bars, the variance, as well as the sample size." (emphasis added) . . . .
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> 235. But before the Patent Office, in a manner wholly inconsistent with Jazz's representations to the FDA that the performance of the two test compounds was "consisten[t]" across studies and that any differences were "slightly smaller," Mr. Allphin and Jazz misrepresented those same data was showing differences which were characterized as, e.g., "***substantially lower***" and "unexpectedly found," and that those results "could not have been predicted by the prior art." JPIL0I 79358

> ('373 patent FH April 8, 2022 Argument/Remarks) (emphasis added). The Patent Office relied on those representations, expressly acknowledging them among the reasons for the allowance of the issued claims of the '373 patent. *See* JPIL0I 79416 ('373 patent FH, May 9, 2022 Notice of Allowance at 2) ("Reasons for Allowance .. . the prior art does not teach the presently-claimed methods provide the unexpected result that there is a reduced food effect in patients ... "). These contradictory assertions represent a clear violation of Mr. Allphin's and Jazz's duty of disclosure.

Defendants' proposed Counterclaim asserts two related theories based on factual allegations about differences between submissions to the FDA and submissions to the PTO. The principal theory contends that the submission to the FDA, but not to the PTO, of the variability data for Figure 1 (the "error bars") supports a claim of inequitable conduct. The second and related theory contends that differences in characterizations of the reduced food effect between submissions to the FDA and to the PTO supports a claim for inequitable conduct. This second theory is a bit difficult to pin down, but Defendants seem to hint that the differences support an inference that the reduced food effect is either so small as to be trivial or perhaps nonexistent; Defendants suggest that the applicants misrepresented the true magnitude of the reduced food effect. Both theories share the proposition that the applicants withheld material information from the PTO with an intent to deceive.

As to both these theories that the applicants engaged in inequitable conduct during prosecution of the '373 patent by withholding particular material information that had been submitted to the FDA as part of the related new drug application, the Court finds that the proposed Counterclaim does not plead sufficient facts to make plausible the inference that the omitted information was material. Nor does Defendants' opening brief state any theory that makes plausible the inference that, had the applicants presented the omitted information to the PTO, the claims would not have been allowed. Defendants' brief merely asserts the conclusion

without explanation: "Withholding the statistical data and proffering contrary conclusions was material because the USPTO would not have allowed the claims of the '373 patent had it been aware of those data and contrary representations." (Defs.' Br. at 32.) The brief, in support, cites 6 paragraphs in the proposed Counterclaim. Defendants' opening brief goes on to say:

> Thus, the removal of the statistical data and misrepresentation of differences in food effect as "substantial" to the USPTO, while describing the same difference to the FDA as "slightly smaller" with the same data showing that "the overall trends are the same" is clearly material. This is evident from the Examiner's stated Reasons for Allowance, stating that Jazz demonstrated that the alleged difference in food effect "was unexpected based on the prior art."

(Defs.' Br. at 33.) Again, Defendants assert the conclusion ("clearly material") without making any argument in support. The facts pled in support of the proposed Counterclaim do not make it plausible that, had the applicants provided the PTO with a copy of Figure 1 that showed the "error bars," the claims would not have been allowed. Nor does Defendants' brief shed any new light on the matter.

The Court inquires: what about including the error bars in Figure 1 would make it plausible that, because of the presence of the error bars, the PTO would not have allowed the claims? Defendants offer only conclusory assertions of but-for materiality, rather than pleading facts that make the inference plausible. It is a simple fact that Defendants never explain how and why the presence of the error bars, or any characterization of the magnitude of the reduced food effect, might have affected the PTO's decision to allow the claims.[1]

[1] In opposition, Plaintiff observes that, in October of 2023 in the instant litigation, Defendants filed a Markman brief that relies on a detailed discussion of the finding of a reduced food effect based on the data in Table 4 in the patent. (See Docket Entry No. 98 at 4.) Defendants' Markman brief asserts that, in short, the reduced food effect is shown by a simple calculation using the data in Table 4. (Id.) Plaintiff contends that Defendants' position on this motion is inconsistent with its earlier position, but does not argue that Defendants should be judicially

Defendants never articulate what the error bars might have suggested to the PTO. Instead, they shine the spotlight on the word "reliability" but neither plead facts nor offer explanations that make plausible the inference that variability measures for the C_{max} values displayed in Figure 1 and Table 4 would have changed the PTO's determination to allow the claims. What is the connection between the variability data and the determination to allow the claims? No facts have been pled which make plausible an inference that the PTO would not have allowed the claims had it known about the variability of the C_{max} values in Figure 1.[2] Defendants rely on conclusory assertions only.

The proposed Counterclaim alleges that, by omitting the error bars, "Mr. Allphin misleadingly presented the data to the Patent Office." (Proposed Am. Answer at ¶ 231.) Again, the word "misleadingly" here is both conclusory and vague. Defendants do not explain how Figure 1 and Table 4 misled the PTO. It is important to note that at no point do Defendants contend that the data presented in Figure 1 are false. The proposed Counterclaim alleges that Allphin told the FDA that "the data provides strong evidence that [the inventive] oxybate solutions . . . are subject to slightly smaller food effects than Xyrem." (Proposed Am. Answer at

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estopped from advancing the inconsistent position. It is nonetheless worth noting that, at that point in the litigation, Defendants offered simple calculations to show that the data in Table 4 demonstrates the reduced food effect. In the Markman brief, Defendants did not argue that, to demonstrate the reduced food effect, variability data is needed. Thus, to the extent that Defendants now suggest that the reduced food effect is trivial or non-existent, this position is inconsistent with Defendants' argument in the Markman brief that the reduced food effect was easily demonstrated by simple calculations using the data from Table 4.

[2] The Counterclaim alleges that Allphin testified: "in order to know how reliable data are, you'd have to know two things; the error bars, the variance, as well as the sample size." (Proposed Am. Answer at ¶ 231.) The proposed Counterclaim pleads no facts that make plausible the inference that the reliability of the Figure 1 data was material to the PTO decision to allow the claims. What is the connection between the variability data and the PTO determination of unexpected results?

¶ 234.) Defendants do not explain why, had Allphin made this statement to the PTO, it might plausibly have changed the outcome. Claim 1 of the '373 patent requires that the composition has "reduced food effect as measured by C_{max} compared to an equal dose of [the Xyrem composition]." Defendants have offered this Court no basis to find it plausible that the presence of the error bars, or any characterization of the magnitude of the reduced food effect, would have changed the PTO's determination that the reduced food effect results were unexpected.[3]

Defendants argue that the alleged omission of the error bars is "*per se* material" under MPEP § 2001.06(e). That section of the MPEP, however, which deals with documents submitted to regulatory review bodies such as the FDA, expressly restricts its scope to documents material to patentability. As already explained, the proposed Counterclaim does not allege facts that make plausible the inference that the applicant withheld documents material to patentability.

As to the second theory, Defendants' brief hints that Allphin misled the PTO about the magnitude of the difference in the food effect for the inventive composition compared to Xyrem.[4] Again, however, the proposed Counterclaim pleads no facts to make plausible the

[3] A "slightly smaller food effect" would appear to constitute a reduced food effect, as required by claim 1.

[4] Defendants also suggest that Federal Circuit law requires a "marked superiority" in the unexpected property to constitute an unexpected result sufficient to rebut the *prima facie* case of obviousness, citing Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc., 752 F.3d 967, 977 (Fed. Cir. 2014). The Federal Circuit, however, has made clear that there are no such bright-line rules in this inquiry, and even the general principle stated in Bristol-Myers does not impose such a requirement: "To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention." Id. In a more recent case which cited Bristol-Myers, the Federal Circuit compared a "20-fold" (20 times greater) difference in drug potency to a "two-fold" (2 times greater) difference, and held:

inference that the magnitude of the reduction in the food effect was material to patentability. Defendants point to the statement made by the Examiner in the "Reasons for Allowance" section of the Notice of Allowance, here quoted in its entirety:

> The following is an examiner's statement of reasons for allowance: the prior art does not teach the presently-claimed methods provide the unexpected result that there is a reduced food effect in patients administered a composition having the claimed GHB salt mixture (as exemplified by Formulation O from the present specification) for the treatment of cataplexy or excessive daytime sleepiness with narcolepsy compared to patients administered an equal dose of immediate release liquid solution of Na*GHB (as exemplified by XYREM®). This result of the claimed methods was unexpected based on the prior art.

(Notice of Allowance at 2.) In this statement, the Examiner points to "a reduced food effect." The Examiner did not refer to the magnitude of the reduction. The proposed Counterclaim pleads no facts that make plausible that the magnitude of the reduction was material to the Examiner's decision to allow the claims. Defendants' opening brief does not directly state that the applicant's assertion of a reduced food effect was a falsehood.

Moreover, to the extent that Defendants assert their second theory that the applicants deceived the PTO about the magnitude of the reduced food effect, Plaintiff points out that this is inconsistent with the position taken by Defendants in their Markman brief filed earlier in this case.[5] Not only is the denigration of the size of the effect inconsistent with the previous position,

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> There is no specific fold-difference that defines what may, or may not, support a finding of nonobviousness. Nor do we draw a line between a difference in degree insufficient to rebut a showing of obviousness and a difference in kind that may be sufficient to do so; each inquiry need be fact-specific. *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014).

Amgen Inc. v. Sandoz Inc., 66 F.4th 952, 964 (Fed. Cir. 2023).

[5] In the Markman brief, Defendants wrote: "This 'reduced food effect' of the mixed-salt GHB as compared to Xyrem® is shown in Table 4 of the '373 patent." (Defs.' Markman Br. at 4.)

but Defendants' reply brief failed to challenge a key assertion in Plaintiff's opposition: "Under Defendants' own analysis, all information required to determine whether the claimed formulation did, in fact, have a reduced food effect compared to Xyrem is provided in the '373 patent itself." (Pl.'s Opp. Br. at 11.) The Court construes Defendants' failure to challenge this in reply as a concession that the assertion is correct, and that the patent contains all information needed to determine the existence of the asserted reduced food effect. When they filed the Markman brief, Defendants appeared to believe that the data in the patent were sufficient to demonstrate the reduced food effect. To the extent that Defendants now hint that the reduced food effect does not really exist, they have changed their position.

Defendants contend that this case resembles that of Belcher Pharms., LLC v. Hospira, Inc., 11 F.4th 1345, 1347 (Fed. Cir. 2021), in which the Federal Circuit affirmed the district court's decision that a party had engaged in inequitable conduct by withholding material information from the PTO during patent prosecution. The Federal Circuit held:

> A prior art reference may constitute material information, even where the reference is not sufficient to invalidate the claim in district court, if the disclosure of the reference would have blocked the issuance of a patent under the PTO's evidentiary standards. Thus, prior art is but-for material information if the PTO would not have allowed a claim had it been aware of the undisclosed prior art. The standard for establishing but-for materiality in the inequitable conduct context only requires a preponderance of the evidence, giving claims their broadest reasonable construction.
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> [Appellant] does not challenge the district court's decision that the asserted claims are invalid as obvious based on, *inter alia*, JHP's epinephrine product, testing of which showed the product had a pH within the claimed range. Because that is the case, the product is "necessarily material to patentability." *Aventis*, 675 F.3d at 1334; *see also Therasense*, 649 F.3d at 1276 ("[I]f a claim is properly invalidated in district court based on the deliberately withheld reference, then that reference is necessarily material because a finding of invalidity in a district court requires clear and convincing evidence, a higher evidentiary burden than that used in prosecution at the PTO.")

Belcher Pharms., LLC v. Hospira, Inc., 11 F.4th 1345, 1352-53 (Fed. Cir. 2021) (citations omitted.) The facts of the instant case are not analogous to those of Belcher: here there is no uncontested prior determination of patent invalidity that necessitates the determination of materiality. Instead, in the instant case, Defendants have not pled sufficient facts to make plausible the inference of materiality.

A more relevant case for comparison is Helsinn Healthcare S.A. v. Teva Pharms. USA, Inc., 855 F.3d 1356, 1372 (Fed. Cir. 2017), in which the Federal Circuit distinguished between the standard that governs FDA approval of new drugs and the standards that govern patent law. In short, the Federal Circuit made the point that the two are very different and that the FDA applies a "more demanding standard" during the new drug approval process than the PTO applies during patent prosecution. Id. Although the issue in Helsinn was reduction to practice, rather than unexpected results, as in the instant case, the Federal Circuit's discussion of that standard is useful in thinking about this case:

> In patent law, the requisite testing, if any, for showing that an invention will "work for its intended purpose" varies depending on "the character of the invention," including the claim language and the "nature and complexity of the problem" the invention seeks to solve. Generally there must be some "demonstration of the workability or utility of the claimed invention." This must show that the invention works for its intended purpose "beyond a probability of failure" but not "beyond a possibility of failure."

Id. (citations omitted).

The preamble of claim 1 of the '373 patent is "a method of reducing food effect due to administration of [GHB]." The intended purpose of claim 1, thus, is reducing the food effect due to administration. Under Helsinn, patent law requires only "some demonstration" that the invention works for its intended purpose. Helsinn teaches that patent law does not apply the

demanding standard that the FDA applies during the new drug approval process. Thus, the mere fact that Plaintiff and/or the applicants submitted different applications to the FDA and to the PTO does not, alone, make plausible any inference of misconduct. As the Federal Circuit explained in Helsinn, the standards applied by the FDA to new drug applications and the standards applied by the PTO to patent applications are different. 855 F.3d at 1372. Nor do the facts pled make plausible the inference that the relative magnitude (substantial vs. slight) of the reduction in food effect would have been material to patentability.

As already stated, the Federal Circuit's law on inequitable conduct requires proof of both materiality and intent. As to the intent requirement:

> To prevail on a claim of inequitable conduct, the accused infringer must prove that the patentee acted with the specific intent to deceive the PTO. A finding that the misrepresentation or omission amounts to gross negligence or negligence under a "should have known" standard does not satisfy this intent requirement. . . [T]he accused infringer must prove by clear and convincing evidence that the applicant knew of the reference, knew that it was material, and made a deliberate decision to withhold it. . . .
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> Intent and materiality are separate requirements. . . . Moreover, a district court may not infer intent solely from materiality. Instead, a court must weigh the evidence of intent to deceive independent of its analysis of materiality. Proving that the applicant knew of a reference, should have known of its materiality, and decided not to submit it to the PTO does not prove specific intent to deceive.
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> Because direct evidence of deceptive intent is rare, a district court may infer intent from indirect and circumstantial evidence. However, to meet the clear and convincing evidence standard, the specific intent to deceive must be "the single most reasonable inference able to be drawn from the evidence." Indeed, the evidence "must be sufficient to require a finding of deceitful intent in the light of all the circumstances." Hence, when there are multiple reasonable inferences that may be drawn, intent to deceive cannot be found.

Therasense, 649 F.3d at 1290-91 (citations omitted).

As to the error bars and the element of intent, Defendants' inequitable conduct theory rests on the contention that the applicants intended to mislead and deceive the PTO. In short, the Court finds that the facts alleged do not suffice to make that inference plausible, for several reasons. No factual allegations make plausible the inference that the applicants knew that the error bars were material to patentability. Nor is intent to deceive the PTO by deliberately withholding the error bars the single most reasonable inference to be drawn from the allegations.

The proposed Counterclaim alleges that the applicants submitted the results in Figure 1 and Table 4; it is apparent that these results do not contain any data about the variability of the C_{max} data. The PTO allowed the claims and issued the patent. No facts make plausible the inference that the applicants deliberately withheld the error bars with the specific intent to deceive the PTO. Certainly such an inference is not the most reasonable inference able to be drawn from the facts alleged.

The specification of the '373 patent expressly references the FDA's standard for food effect studies, "('Guidance for Industry: Food-Effect bioavailability and Fed Bioequivalence Studies', FDA December 2002)." '373 patent, col.36 ll.15-19. The specification also specifically references the FDA standard for bioequivalence within the definition of "bioequivalent." '373 patent, col.11 l.59-col.12 l.17. The parties have not disputed the correctness of the applicants' application of these FDA bioequivalence standards to the data disclosed in the patent. Nor have Defendants alleged that either the FDA food effect study standards or the FDA bioequivalence standards require analysis of the error bars or C_{max}

variability data.[6] The factual allegations in the proposed Counterclaim do not make plausible that, by omitting the error bars in Figure 1, the applicants intended to deceive the PTO.

As to the suggestion that the applicants misrepresented the magnitude of the reduced food effect, the factual allegations fail to make plausible that any such actionable misrepresentation occurred. The facts alleged do not support an inference that the applicants intended to deceive the PTO.

II. The theory of inequitable conduct based on omitting Wilding's prior art references

Defendants propose a second theory of inequitable conduct based on the allegation that the applicants withheld material prior art references, based on the Ian Wilding email.[7] (See Proposed Am. Answer at ¶¶ 238-249.) In short, Defendants allege that Wilding alerted Allphin to a number of prior art references that would have been material to patentability and which the applicants withheld during prosecution. The proposed Counterclaim alleges that the Wilding references would have demonstrated to the PTO that the reduced food effect was predictable. There are several problems with this second theory.

First, the facts alleged in support of the second theory fail to make plausible that, but for the omission of a particular cited reference, or combination of references, the claims would not

[6] Rather, in the end, Defendants ask this Court to consider the allegation that different information was submitted in applications for different purposes to the FDA and to the PTO, and to find that this makes plausible an inference of inequitable conduct. It does not suffice to do so.

[7] The proposed Amended Answer references the Wilding email, which is an exhibit to the Walsh Declaration accompanying Defendants' moving brief; the Court considers the Wilding email to have been incorporated into the proposed Amended Answer by reference. Tellabs, Inc. v. Makor Issues & Rts., Ltd., 551 U.S. 308, 322 (2007) ("courts must consider the complaint in its entirety, as well as other sources courts ordinarily examine when ruling on Rule 12(b)(6) motions to dismiss, in particular, documents incorporated into the complaint by reference, and matters of which a court may take judicial notice.")

have been allowed. Neither the proposed Counterclaim nor Defendants' brief offers more than a vague and conclusory assertion that the but-for materiality standard has been met. Defendants do not explain how the referenced prior art references make plausible the inference that, had the PTO known about one or more of them, it would have found the claims unpatentable as obvious.[8] The proposed Counterclaim suggests that these references would have precluded the PTO's conclusion of unexpected results by demonstrating that the reduced food effects were predictable.

A shortened version of Defendants' proposed allegations about Ian Wilding and the prior art references he cited follows:

> 237. Third, Mr. Allphin failed to disclose material references and prior art that would have provided the Examiner with a better understanding of the prior art as a whole and that the claimed food effect was, in fact, predictable.
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> 238. In an email dated December 11, 2015, on with [*sic*] Mr. Allphin was copied, Jazz requested that Ian Wilding of Ian Wilding Associates, assess and comment on the purportedly observed food effects. Three days later, in an email dated December 14, 2015, Ian Wilding provided an assessment that explained away the observed differences in PK parameters between Xyrem and Xywav, which Ian Wilding believed was based on the magnesium content of the mixed salt formulation. JPIL0085254. He attached a half dozen references to support his theories, none of which were provided to the patent attorneys or the USPTO. *Id.*
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> 243. [] Ian Wilding explained that the prior art taught that inclusion of a magnesium salt would have changed the body's digestion of the claimed formulation versus one comprised of sodium oxybate.

[8] Compare Belcher. Defendants' reference to Belcher highlights what is missing in the instant case. In Belcher, the district court had already found the claims obvious over the withheld reference. Belcher, 11 F.4th at 1352. Not so here. Nor have Defendants plausibly alleged that, had the Wilding references been disclosed to the PTO, the claims would have been rejected as obvious.

(Proposed Am. Answer.) The allegations that follow contend that the omitted references concern research on the effect of magnesium on intestinal transit time (as well as the effect of the excipient mannitol, the relevance of which is unexplained.)

Applying the Rule 12(b)(6) standard, this Court takes these factual allegations as true in the futility analysis. The bottom line of Defendants' theory of the omitted Wilding email references is that "the claimed food effect was, in fact, predictable." (Proposed Am. Answer at ¶ 237.) The Court finds that the facts alleged, taken as true, do not make plausible that inference because Defendants fail to take into account all of the research and results disclosed in the patent specification. In short, Defendants propose that the prior art studies on the effect of magnesium on intestinal transit time enabled a POSA to predict the reduced food effect disclosed in Example 2.1 and Table 4. As will be explained in the discussion that follows, the Court does not find the allegations sufficient to make this inference plausible but, even if it did, Defendants' theory also fails more obviously because of the results disclosed in Example 2.3 and Table 6. As Plaintiff points out, in short, the results in Example 2.3 and Table 6 rebut Wilding's theory about the role or effect of magnesium.

Plaintiff describes the results of bioequivalence Study 1 as follows:

> Study 1 showed that the mixed-salt formulations were not bioequivalent to Xyrem under FDA standards, meaning that the "geometric mean of . . . the Cmax" did not meet the statistically significant value of "between 80% and 125% (e.g., at 90% confidence interval) of the reference pharmacokinetic value." Study 1, part 1 further showed that Xywav had a reduced food effect compared to Xyrem. While the two had a bioequivalent Cmax in the fed state, they did not in the fasted state. Instead, the Cmax for Xywav was "significant[ly] and substantial[ly]" lower compared to Xyrem in the fasted state.

(Pl.'s Opp. Br. at 6) (citations omitted). Then, Plaintiff describes the results of bioequivalence Study 2:

> Study 2 looked at multiple different oxybate cation salt mixtures "[t]o test for negative effects of certain cations." Those 2016 experiments empirically disproved the consultant's 2015 theory regarding magnesium. Study 2 investigated two different formulations without magnesium—one with 50% sodium (507-D) and one with 33% sodium (507-A). Only "[f]ormulation 507-D with 50% sodium met the bioequivalence criteria." Formulation 507-A, also without magnesium, was not bioequivalent.

(Pl.'s Opp. Br. at 7) (citations omitted). Table 6 states that the formulations in Study 2 were tested in the fasted state.

Defendants' reply brief did not challenge Plaintiff's opposition brief description of the specification disclosures about Study 1 and Study 2. Thus, the Court finds that Examples 2.1 and 2.3 in the patent specification, including Tables 4 and 6, disclose: 1) Xywav, which contains magnesium, was bioequivalent to Xyrem in the fed state and not bioequivalent in the fasted state; and 2) of two alternative formulations without magnesium, one was bioequivalent to Xyrem in the fasted state and one was not bioequivalent in the fasted state. As Plaintiff contends, the presence or absence of magnesium in the formulation does not appear to predict the bioequivalence results disclosed in Study 1 and Study 2 in the specification.[9] The factual allegations in the proposed Counterclaim do not make plausible the inference that the claimed food effect, together with the subsequent studies, was predictable from the prior art studies of the effect of magnesium on intestinal transit time.[10]

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[9] Example 2.3 states that both formulations 507-C, which has magnesium at a level close to that in Xywav, and formulation 507-A, with no magnesium, were not bioequivalent to Xyrem®. Also, formulation 507-D, with no magnesium, was bioequivalent to Xyrem®. These results are not consistent with Defendants' theory that the simple presence or absence of magnesium predicts bioinequivalence. It is not plausible that Defendants' magnesium theory accounts for all of the variations in bioinequivalence results disclosed in the patent specification.

[10] Moreover, while it can be debated whether the Court on this motion may consider the entire email chain between Allphin and Wilding (contained in Sullivan Dec. Ex. 7), the Court notes that the email chain in Exhibit 7 indicates that Wilding subsequently stated: "There is a clear

The Court also questions the relevance and significance of Wilding's opinion to the question of whether the results were unexpected. Even if the Court considers only the reduced food effect in isolation, without the additional studies in Example 2.3, Wilding's opinion with his prior art references appears to be textbook hindsight analysis of obviousness. Defendants do not articulate a theory to explain how the references cited by Wilding meet the but-for materiality standard and the Court is left wondering, how does this hindsight commentary on the results of a food effect study establish that the results were predictable and the invention obvious? Courts are frequently offered hindsight explanations of inventions, and the Federal Circuit has warned about the dangers of relying on them:

> Indeed, where the invention is less technologically complex, the need for *Graham* findings can be important to ward against falling into the forbidden use of hindsight. Simply because the technology can be easily understood does not mean that it will satisfy the legal standard of obviousness. In fact, objective consideration of simple technology is often the most difficult because, once the problem and solution appear together in the patent disclosure, the advance seems self-evident. Instead, the proper analysis requires a form of amnesia that "forgets" the invention and analyzes the prior art and understanding of the problem at the date of invention.

Mintz v. Dietz & Watson, Inc., 679 F.3d 1372, 1379 (Fed. Cir. 2012). The Wilding analysis is hindsight, tracing backwards from the invention to the prior art.

Moreover, Defendants have not explained how, applying the law of obviousness to these factual allegations, one or more of the Wilding references would have resulted in a conclusion of obviousness. Consider the Supreme Court's teaching about the obviousness analysis in KSR:

> The principles underlying these cases are instructive when the question is whether a patent claiming the combination of elements of prior art is obvious. When a

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dose dependent lowering of C_{max} as you increase the amount of Mg/Ca/K in the mix." In this comment, Wilding appears to acknowledge that the effect on C_{max} is related not only to the presence of magnesium, but also calcium and potassium.

> work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variation, § 103 likely bars its patentability. For the same reason, if a technique has been used to improve one device, and a person of ordinary skill in the art would recognize that it would improve similar devices in the same way, using the technique is obvious unless its actual application is beyond his or her skill. *Sakraida* and *Anderson's-Black Rock* are illustrative--a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions.
>
> Following these principles may be more difficult in other cases than it is here because the claimed subject matter may involve more than the simple substitution of one known element for another or the mere application of a known technique to a piece of prior art ready for the improvement.

KSR Int'l Co. v. Teleflex Inc., 550 U.S. 398, 417 (2007). The Court considers the proposed allegation that the claimed food effects were predictable based on the prior art in the context of the teachings of KSR. Considering the proposed Counterclaim in the light of KSR, this Court sees no plausible path from the factual allegations to either: 1) a conclusion that the reduced food effect was predictable; or 2) a conclusion of obviousness. What is Defendants' theory of predictability? Is there an unstated theory here that starts with a lead compound and a string of obvious, predictable variations to it? What would the lead compound have been and why? If the lead compound was sodium oxybate, what suggested replacement of some sodium in sodium oxybate with magnesium, and on what basis could this be considered a predictable variation? What of the fact that the composition of claim 1 includes sodium, potassium, calcium and magnesium ions? How was the result predictable based on Wilding's prior art references about the effect of magnesium alone? The point is that the proposed Counterclaim offers a few prior art references that were not disclosed by the applicants but gives the Court no basis to find that the factual allegations make plausible that, but for the withholding of these references, the claims would not have been allowed.

For the purpose of the futility analysis, the Court accepts as true the allegations that the prior art contained a number of specific references which taught that magnesium can accelerate intestinal transit time. The legal issue for the counterclaimant is whether the factual allegations make plausible the inference of but-for materiality, and the Court finds that the allegations about the Wilding email and references do not make but-for materiality plausible. Defendants contend that a POSA would have expected that the inventive composition would have a reduced food effect, based on what these references teach about magnesium and intestinal transit time. The problem here is that this a hindsight-based, cherry-picked view of what appears to be a much more complex and difficult question, because the inventors did not simply take the prior art sodium oxybate and simply substitute magnesium or simply add magnesium. Instead, the inventors claimed a genus of compositions that combine sodium oxybate, potassium oxybate, calcium oxybate, and magnesium oxybate in varying proportions, and the facts alleged do not make plausible that the prior art POSA would have had any particular expectation about the impact of such a combination on the effect of food on oral administration. In short, if we liken the result obtained (reduced food effect) to a jigsaw puzzle with at least several pieces, the Wilding email at best makes plausible that the prior art POSA would have possessed one puzzle piece out of the group that would make plausible the results obtained.

Even this analysis, however, does not adequately address the complexity of the problem because, as Plaintiff points out in opposition, the patent specification reports a study with results that rebut Wilding's theory. Plaintiff's opposition brief discusses at length the three bioequivalence studies that the patent specification reports in Example 2. (Pl.'s Opp. Br. at 5-8.) Example 2.3 describes a bioequivalence study in which several alternative cation blends were

tested for bioequivalence with Xyrem®. As shown in Table 6 in the specification, there were two formulations without magnesium; one was found to be bioequivalent to Xyrem® but the other was not. This data weighs heavily against finding that prior art knowledge of magnesium on intestinal transit time plausibly predicted the bioequivalence failure of the inventive composition in the fasted state.

As to the element of specific intent to deceive the PTO, again, as explained with regard to the error bars theory, no facts make plausible the inference that the applicants deliberately withheld the Wilding email prior art references with the specific intent to deceive the PTO. Certainly such an inference is not the most reasonable inference able to be drawn from the facts alleged, viewed in the context of the patent in its entirety. Given the results in Table 6, which suggest that Wilding's theory did not fit all of the relevant data, it is not plausible that the applicants believed that the Wilding references were material and intended to deceive the PTO by withholding them.

The Court concludes that, for the reasons stated, the proposed Counterclaim would not survive a motion to dismiss under Rule 12(b)(6). The proposed allegations do not plausibly give rise to an entitlement to relief on an inequitable conduct counterclaim for any of the theories raised by Defendants: the omission of the error bars, the alleged variations in characterizations of the magnitude of the reduced food effect, and Wilding's magnesium prior art references. For none of these theories do the proposed allegations make plausible the two elements of a claim for inequitable conduct, but-for materiality and specific intent to mislead or deceive the PTO. Amendment of the Answer to include the proposed inequitable conduct Counterclaim is futile. The motion for leave to amend the Answer will be denied.

In opposition, Plaintiff argues that, additionally, the motion to amend should be denied because Defendants do not meet the requirements of Local Patent Rule 3.7, which states: "Amendment of any contentions, disclosures, or other documents required to be filed or exchanged pursuant to these Local Patent Rules may be made only by order of the Court upon a timely application and showing of good cause." See O2 Micro Int'l, Ltd. v. Monolithic Power Sys., 467 F.3d 1355, 1366 (Fed. Cir. 2006) ("'good cause' to amend requires a showing of diligence. . . The burden is on the movant to establish diligence.") Plaintiff contends that Defendants have failed to establish the diligence necessary to support a finding of good cause. Defendants, in reply, point to emails between counsel for the parties about document discovery from May and June of 2024 (Walsh Reply Dec. Ex. A) and contends: "To the extent that there was a delay in noticing Mr. Allphin's (and other inventor's) depositions, it is a direct result of Jazz's own delays in producing documents directly implicating Mr. Allphin, among the other Jazz inventors." (Defs.' Reply Br. at 3.) While that email chain confirms that document discovery continued into the summer of 2024, Defendants do not point to any specific document that was disclosed in 2024 that triggered their effort to depose Allphin.

Plaintiff, on the other hand, contends:

> Jazz produced all of the documents on which Defendants base their claims to Defendants by July 2023 (for Lupin) and December 2023 (for Teva). Those are the '373 patent, the '373 patent file history, the bioequivalence studies, the FDA Package, and the December 2015 consultant email and associated references. Everything Defendants plead is readily apparent from the face of those documents. Defendants did not need Allphin's deposition to see that the '373 patent figures do not have error bars like the FDA Package. Nor did they need Allphin's deposition to see that the consultant sent his email in December 2015 and that Allphin reviewed (and commented upon) it then.

(Pl.'s Opp. Br. at 19.) Defendants' reply brief did not dispute Plaintiff's statement about the specific relevant documents that Plaintiff contends were produced by December of 2023 at the latest.

The Court finds Defendants' argument unpersuasive. The patent file wrapper and the FDA Package should have given Defendants the basis to find that the applicant submitted Figure 1 to the PTO without the error bars that had been disclosed to the FDA. The file wrapper also contains the Applicant-Initiated Interview Summary for the February 16, 2022 interview with the Examiner, which lays out the applicants' position about the evidence of unexpected results, as well as the Reasons for Allowance contained in the Notice of Allowance, which explains that the evidence of unexpected results provided the basis for the PTO decision to allow the claims. When Defendants had those documents, Defendants had the basis to initiate discovery into the question of who was responsible for the creation and submission of Figure 1 to the PTO. The Court is not persuaded that Defendants acted with the requisite diligence in its pursuit of this inquiry. This motion was filed in October of 2024. Defendants have failed to establish the diligence necessary for this Court to find the good cause required by L. Pat. R. 3.7.

Defendants' motion to amend will be denied.

For these reasons,

IT IS on this 18th day of February, 2025

ORDERED that Defendants' motion for leave to amend the Answer (Docket Entry No. 184) is **DENIED**.

s/ Stanley R. Chesler
STANLEY R. CHESLER
United States District Judge